IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICANT	: Jackowski *et al.*
INVENTION	: **Protein Biopolymer Markers Predictive of Type II Diabetes**
SERIAL NUMBER	: 09/993,393
FILING DATE	: November 23, 2001
EXAMINER	: Cook, Lisa V.
GROUP ART UNIT	: 1641
OUR FILE NO.	: 2132.110

CERTIFICATE UNDER 37 CFR 1.8(a)
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DECLARATION UNDER 37 CFR § 1.132

I, Ferris H. Lander, do hereby declare as follows:

1. I am a registered Patent Agent and am authorized to represent the inventor's and assignee in the application entitled **"Protein Biopolymer Markers Predictive of Type II Diabetes"**, having U.S. Application Serial No. 09/993,393, filed November 23, 2001.

2. In the Final Office Action mailed on July 26, 2005, claim 1 (as presented on May 9, 2005) was rejected under 35 USC 101 because the claimed invention allegedly is not supported by either a specific, substantial, credible or asserted utility or a well-

established utility. Claim 1 was also rejected under 35 U.S.C. 112, first paragraph because the claimed invention allegedly contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, the Examiner asserts that the figures do not show clear differential expression of the claimed peptide (SEQ ID NO:4) between normal patients and Type II diabetes patients; thus, a link or association between the claimed sequence (SEQ ID NO:4) and Type II diabetes is not exemplified in the disclosure.

3. The attached figure was produced by scanning the original photograph of the gel. The figure is entitled "HiQ3 (scrub) Normal vs. Diabetes Type II" and represents Figure 1 as originally filed. No new matter has been added; this figure is simply a clearer copy of Figure 1 as originally filed and is provided to clarify the differential expression of the claimed biopolymer marker (SEQ ID NO:4); i.e., to clarify the presence of Band 3 (from which the claimed peptide, SEQ ID NO:4, was isolated) in samples obtained from Type II diabetes patients and the absence of Band 3 in samples obtained from patients determined to be normal with regard to Type II diabetes. The gel shown in the figure does not represent new experimentation; the figure shows a clearer image of the original gel made at the time that the experiments described in the instant specification were first carried out.

The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the Application or any patent issuing thereon.

11/21/2005
Date

Ferris H. Lander
Reg. No. 43,377

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2132.110 reference # 1

1: J Neural Transm. 1996;103(4):433-46.

Elevated 5-S-cysteinyldopamine/homovanillic acid ratio and reduced homovanillic acid in cerebrospinal fluid: possible markers for and potential insights into the pathoetiology of Parkinson's disease.

Cheng FC, Kuo JS, Chia LG, Dryhurst G.

Department of Medical Research and Geriatrics Medical Center, Taichung, Taiwan, Republic of China.

High-performance liquid chromatography with electrochemical detection has been employed to analyze ultrafiltrates of cerebrospinal fluid of Parkinson's Disease (PD) patients and age-matched controls for the dopamine (DA) metabolites homovanillic acid (HVA) and 5-S-cysteinyldopamine (5-S-CyS-DA). The mean level of HVA in the CSF of PD patients, measured 5 days after withdrawal from L-DOPA therapy, was significantly lower than that measured in controls. By contrast, mean levels of 5-S-CyS-DA were not significantly different in the CSF of PD patients taking L-DOPA (PD-LT patients) the same patients 5 days after discontinuing this drug (PD-LW patients) or controls. However, the mean 5-S-CyS-DA/HVA concentration ratio was significantly ($p < 0.05$) higher in the CSF of PD-LW patients compared to controls. Although the PD patient population employed in this study had been diagnosed with the disease several years previously and had been treated with L-DOPA for prolonged periods of time the results of this study suggest that low CSF levels of HVA and a high 5-S-CyS-DA/HVA ratio together might represent useful markers for early diagnosis of PD. The high 5-S-CyS-DA/HVA ratio observed in the CSF of PD-LW patients also provides support for the hypothesis that the translocation of glutathione or L-cysteine into neuromelanin-pigmented dopaminergic cell bodies in the substantia nigra might represent an early event in the pathogenesis of PD.

PMID: 9617787 [PubMed - indexed for MEDLINE]

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2132.110 reference #2 Examiner copy

1: Arch Neurol. 1999 Jun;56(6):673-80.

Comment in:

- Arch Neurol. 1999 Jun;56(6):655-6.

FREE TEXT AT ARCHIVES OF NEUROLOGY

Cerebrospinal fluid beta-amyloid(1-42) in Alzheimer disease: differences between early- and late-onset Alzheimer disease and stability during the course of disease.

Andreasen N, Hesse C, Davidsson P, Minthon L, Wallin A, Winblad B, Vanderstichele H, Vanmechelen E, Blennow K.

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OBJECTIVES: To study the diagnostic potential of the 42 amino acid form of beta-amyloid (beta-amyloid(1-42)) in cerebrospinal fluid (CSF) as a biochemical marker for Alzheimer disease (AD), the intra-individual biological variation of CSF-beta-amyloid(1-42) level in patients with AD, and the possible effects of differential binding between beta-amyloid and apolipoprotein E isoforms on CSF-beta-amyloid(1-42) levels. DESIGN: A 20-month prospective follow-up study. SETTING: Community population-based sample of consecutive patients with AD referred to the Pitea River Valley Hospital, Pitea, Sweden. PATIENTS: Fifty-three patients with AD (mean +/- SD age, 71.4 +/- 7.4 years) diagnosed according to the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association criteria and 21 healthy, age-matched (mean +/- SD age, 68.8 +/- 8.0 years) control subjects. MAIN OUTCOME MEASURES: Cerebrospinal fluid beta-amyloid(1-42) level--analyzed using enzyme-linked immunosorbent assay--and severity of dementia--analyzed using the Mini-Mental State Examination. RESULTS: Mean +/- SD levels of CSF-beta-amyloid(1-42) were decreased (P<.001) in patients with AD (709 +/- 304 pg/mL) compared with controls (1678 +/- 436 pg/mL). Most patients with AD (49 [92%] of 53 patients) had reduced levels (<1130 pg/mL). A highly significant correlation (r = 0.90; P<.001) between baseline and 1-year follow-up CSF-beta-amyloid(1-42) levels was

found. There were no significant correlations between CSF-beta-amyloid(1-42) level and duration (r = -0.16) or severity (r = -0.02) of dementia. Low levels were also found in patients with mild dementia (Mini-Mental State Examination score, >25). CONCLUSIONS: The sensitivity of CSF-beta-amyloid(1-42) level as a diagnostic marker for AD is high. The intra-individual biological variation in CSF-beta-amyloid(1-42) level is low. Low CSF-beta-amyloid(1-42) levels are also found in the earlier stages of dementia in patients with AD. These findings suggest that CSF-beta-amyloid(1-42) analyses may be of value in the clinical diagnosis of AD, especially in the early course of the disease, when drug therapy may have the greatest potential of being effective but clinical diagnosis is particularly difficult.

PMID: 10369305 [PubMed - indexed for MEDLINE]
